TRANSCRIPT OF PROCEEDINGS

MEDICO-LEGAL SOCIETY OF VICTORIA

THE MELBOURNE CLUB

MELBOURNE

SATURDAY 12 OCTOBER 2013

The Ageing Mind - Protecting your greatest asset through the stresses of anaesthesia & surgery

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MS LYTHGO: I think we should get started or we will never get to eat. Is everybody ready to start? Associate Professor David Scott is the director of anaesthetics at St Vincent's in Melbourne. He is a fellow of both the Australian and New Zealand College of Anaesthetists and of the Faculty of Pain Medicine. He is a counsellor of our college and he is currently director of the Quality and Safety Committee. He graduated from medicine in 1979 and as well as working here with us he's worked in Boston and in Sweden. Frighteningly intelligent as he is I remember him before he went off to Sweden quietly learning to speak Swedish just as a sort of a light relief in between his work at the hospital.

He has researched and published extensively in the area of pain and is a recognised authority. He has a PhD in the neuropharmacology of nerve pain. His other great area of interest and expertise is cognitive outcomes after anaesthesia and surgery, and with Brendan Silbert who is here and Liz Everett he established the centre for anaesthesia and cognitive function at St Vincent's. It is now an internationally recognised centre researching ageing, cognitive decline and the impact of anaesthesia in surgery with world leading collaborations, including with Alzheimer's International.

David will speak to us tonight on a subject that is of great interest and great relevance to a great number of us here tonight, the ageing mind, protecting your greatest asset through the stresses of anaesthesia and surgery. David Scott.

ASSOCIATE PROFESSOR SCOTT: Thanks very much, Marg, if you don't mind I will just quit while I am ahead I think after

that overwhelming introduction, which is mostly untrue of course. I would very much like to thank your society and Marg in particular and Ian Rose for organising this, to invite me to speak to you, and clearly the topic is off target because none of us have any problems with our minds or our mentation, so just think of it in abstract terms if you will. But nonetheless we are interested in what happens to our mind as we grow older, but in particular the events which may shape it and which affect our ability to function in the long term.

Reflecting on the nature of this group, and indeed on the auspicious collective of previous speakers – I happened to glance at the website and it's just frightening to look at the quality and stature of people you've had address you in the past and I humbly apologise for being here. Nonetheless I have no financial conflicts, regrettably, but our group has received research support from a number of funding organisations in Australia, in particular the NHMRC, the National Heart Foundation, and the Australian and New Zealand College of Anaesthetists, so I would acknowledge that without that sort of support this sort of research can't continue.

I hope you can see the graphs as they come up. The thing to note on this graph is it is two lines; there is a flat blue line and the bottom bit accesses years going from 1950 all the way through to 2050, so a hundred years. That blue line represents the number, the world population of those less than five, staying about the same over the next 20, 30 years. The green line is, it is the people who are some of us, few of us, me, who are going to be over 65 or are over 65, and the proportion of blue to

green is changing in an adverse way in the sense that the population of the world is ageing. I think we're all aware of that, the politicians are aware of that, the funding bodies are aware of that, but it is of significant concern to medicine and healthcare.

From the point of view of what we do, which is anaesthesia, and provision of anaesthesia for surgery you need to look at the number of procedures which are being done in Australia related to various specialties, and obviously at the back you won't be able to see it, so I will put it up. And, you know, the most common procedures are endoscopies and gastroscopies, and I won't ask people to put a hand up and say, you know, who has had what, that might be a bit awkward. One of my good friends considers his colonoscopy to be one of the best experiences he's ever had. I think it was the anaesthetic which was the highlight of that. But there are other procedures like lens implants, hip joint replacements and of course coronary artery surgery, and all of these are procedures on an ageing population in particular, and we need to be looking at how those procedures are actually impacting, because the whole aim of doing these sorts of procedures is to improve our quality of life. It is either to make a diagnosis which you can guide therapy or advice, or to actually intervene to improve - improve performance and quality of life.

So why does it matter to anaesthesia? I thank Liz for hunting out this picture. Basically at the moment in 2010, which is not the moment anymore, 13 per cent of our population was 65 years or older, and that 13 per cent received more than a third of all anaesthetics, they had a

third of more of all surgical procedures in our country, and this population is growing, and if you look at this graph you will see that by 2050 the ratio – the orange bars are the percentage of the population over 65, the green-ish short of khaki bars are the percentage of patients having anaesthetics who are over 65, and roughly almost 48 per cent of people is projected to be having anaesthetic if they are over 65 by 2051. So it is a big issue, we need to know that what we're doing for people is in their best interests.

Clearly things have improved. Now, none of you will remember this, it's probably a scene from around – I understand your Society dates back into the 30s, so last century, so this is the sort of scene outside the front of St Vincent's Hospital, the Victorian Civil Ambulance Service, I do not know if any of you remember this, and now it's – you know, hospital medicine is brilliant. It is very sophisticated, it's got blue skies and clouds and ambulances and things like that, so it is much better and it's in colour.

Let's go back to 1775; what would be an ageing person – well, an ageing person in 1775 would be someone over 40, but nonetheless if you managed to survive you would be subject to the most horrible surgical procedures. John Liston performed one, and this is an amputation of a limb, and that knife you can see there is the surgeon's knife for amputating the limb, and it is not subtle. The idea was to do the procedure – this is why we have this talk before dinner – the idea was to do the procedure as quickly and as deftly as possible, and John Liston could to it in under three minutes; it was brilliant. He did

have another claim to fame; as well as being one of the fastest surgeons he is the only surgeon to have had a 300 per cent mortality from a leg amputation, and it happened a bit like this: so he got in there, he was running the clock, sliced off the patient's leg, happened to slice off three of his assistant's fingers, and in the flourish of the knife sliced off the coattails of one of the gentleman who was onlooking. So the patient died of gas gangrene, the assistant was cross contaminated with gas gangrene and died shortly after that, and the gentleman whose coattails were sliced off fainted and died from a heart attack, which was a 300 per cent mortality, but also reflects that the constitution they had then was like of sick goats, it was hopeless.

Anyway moving on from 1775 we came to 1846, the Ether Dome of Massachusetts General Hospital, and the administration of ether, at last a patient could be apparently unconscious, asleep whilst operating on their neck, and this is a famous administration of anaesthesia by – what is his name – Morton, William Morton, thank you. So now anaesthesia in surgery is terrific, we've got all this high technology stuff, we can cannulate just about any vessel in the body, we can all sorts of amazing things, it still all requires anaesthesia. We need to understand now that we can keep people alive and health and comfortable through these procedures are we doing the very best for our patients in that process.

So I will just ask for a little round table here. I want some feedback from you, you the audience, what are your concerns about anaesthesia, in one word, any words describing what might worry you about having an

anaesthetic. If you are going in to have surgery and anaesthesia.

SPEAKER: Losing marbles.

ASSOCIATE PROFESSOR SCOTT: Losing marbles – excellent answer. Dying, waking up, so not waking up I presume, yes. Not going to sleep, so being aware or awake. Yes, anything else? Cardiac arrhythmia – very specific – so something bad with your heart, maybe a heart attack. I am trying to lead into the answers I have already got written down. Anything else?

SPEAKER: Hypoxia.

ASSOCIATE PROFESSOR SCOTT: Hypoxia, brain damage, yes. Sorry? Memory. So that is the thing that Phoebe was talking about too. That is obviously now two people, that's running the highest odds at the moment. So these are the sort of thing – you left off nausea and vomiting and pain, but I think mostly people do, and in fact the surveys that we do on people's perception of what they fear is loss of control, awareness, being awake during a procedure, the experience of pain, nausea and vomiting.

We have got a lot of good things now which can help us manage that. We have got monitors which can monitor what we think might be possibly the depth of anaesthesia. We have got good analgesics, we ave got good anti-emetics, so we can control a lot of these things, but some of the other things that you mentioned were related to the idea of long ongoing injury or disability, heart attacks, some cardiac event. No one mentioned stroke, and of course death. But risk is relative, and whilst addressing one problem you might not address effectively another, and I just want to bring you into that arena.

So in 1996 what is called the MCSPI Group, a large collaborative group of data led by Dennis Mangano in California at that time looked at the effect of Atenolol, with is a Beta blocking drug. Now many of you may be on a Beta blocking drug, it is a drug which slows down your heart rate, decreases your blood pressure, decreases the risk of ischemic heart disease and is a very effective drug for that sort of problem. So why not give it to patients who are at cardiac risk and decrease their likelihood of having heart attacks.

He did this in 200 patients, and just to – because half of you are legal I understand, I just changed it so that 200 clients, just to get the terminology right so we are all on the same page, and followed them up for two years, and what he found was dramatic. There was a 65 per cent reduction in heart attacks in those who had just got this Beta blocking drug at the time of their surgery. Most of it occurred at the initial phase and this changed the face of advice to patients in cardiac surgery. The American Cardiologist Society adopted recommendations. The Head of Cardiology said patients should be considered seriously for having Beta blockers prior to surgery if they are not already on them.

Obviously there was a lot of concern and criticism about this, but this really swept – well, there are a couple of supported studies, but it was not until this article appeared in 2008 as a result of a large multi-centred well researched study looking at the use of Beta blockers for 30 days prior to and following surgery called the POISE study to look at these outcomes. They looked at over 8,000 patients – not 200 patients, 8,000, having

major surgery and what they found was what Mangano had found; not as dramatic as what Mangano had found, but the reduction – there was about a 16 per cent reduction in the incidence of heart attack, almost a 25 per cent reduction in heart attack rate and cardiac event rate was reduced, so the Beta blockers are doing a great job of protecting the heart.

The important thing about looking at information and doing properly conducted studies is they looked at everything. The death rate, the mortality was increased by 30 per cent than those who got Beta blockers. The stroke rate was doubled than those who got Beta blockers. So hands up in the room who would prefer to have no heart attack and a stroke. Okay. So I think the answer is the brain wins, we want to protect our brains.

A heart attack which is not fatal is a terrible thing. It is a high risk event, but it is not as bad as having a stroke or something affecting your brain, your brain is what you are. So the answer to this was that the brain wins, and hopefully most of the brains are better than (indistinct), and that research wins. This is a good example of effective research affecting outcomes and progressing our knowledge of this, but it does make a difficult decision, do you have a Beta blocker or not. I would make a caution here, that if you are already on Beta blockers you stay on your Beta blockers, that is fine, you are going to do fine. Do not put them in the rubbish or anything like that.

So let's bring in the topic, what the topic is about – I have used up three-quarters of my time on nothing in particular – and talk about cerebral insults. So what do

you think, and I am faced with this challenge every day of my life, what do you think is the biggest cerebral insult we are facing in our community today? Wrong. The Kardashians. This tripe is on TV every day and my daughter is watching it.

Moving on, you are right, there are other cerebral insults which we can address more effectively, because there is no way I can tell her to stop watching the show, "But it's good, dad." So stroke is a major insult. Dementia is horrible, it is losing of the mind, and of course cognitive impairment, a more subtle but more pervasive thing which we will talk about in more detail. It is not new. In 1887 a surgeon George Savage published in a British Medical Association a report, so this is only, you know, 40, 50 years after the start of anaesthesias, and noted that there are patients who do not wake up well after their anaesthetic, and in fact although some patients may have a short term temporary mental disorder others may pass into chronic weak-mindedness or even progressive dementia, which is not – cannot be distinguished from general paralysis of the insane, which was the old term senile dementia.

So this was identified in 1887, but we are now in 2013, there can't be that problem anymore. We have got a controlled, we have got a quiet, we have got a stress free operating room, apart from – any surgeons here – apart from the way surgeons behave, but we do get these emails and we do get these communications from people: "I am a 63 year old female, five years ago I had a hip replacement. I was a counsellor prior to this. After the surgery it was like my mind was in cotton wool. My memory

was impaired, my motivation was reduced and I gave up my practice and went into early retirement." "My friend, a clinical psychologist, had extensive surgery as these symptoms only worsened, she is 52 years old." "My father was living independently and caring for my mother. He broke his hip and had it fixed. He is physically the same, but can't remember anything in a short term. He can't adapt to changing environments."

These are extreme adverse cognitive outcomes related to what has happened to these people, and our group was interested in looking into what was underlying all of this, along with many other people. So we have these expectations don't we. We have this expectation of a general – I am going to make some of you a bit uncomfortable here – but general anaesthesia is sleep. Safe. All the legal profession is following the logical argument so far. Therefore anaesthesia is safe. There are common fears and concerns which we have raised, but the brain is the target organ of anaesthetics, and anaesthesia is not sleep. I guarantee you that if you are lying in bed tonight enjoying a restful repose after a nice meal and someone put a scalpel into your stomach you would take notice, you would sit up and pay attention. Now understand anaesthesia is not sleep. It is lack of conscious sensation, it is lack of awareness, it is a medically induced coma.

All this media hype about someone who is put into a medically induced coma anaesthetists do this two million times a year every year in Australia, a tenth of the population has this experience. It is not sleep. It's more than sleep, much more powerful than sleep. We need

to understand more about it. The other thing is that hospitals are not a benign place to be in. You will know if you have had an elderly relative go into hospital. They have got the medical condition you are going into it, it is an unfamiliar environment, it is noisy, it's stressful, there are strangers all around you and it is very easy for older people to decompensate in this sort of environment, and then they have procedures on top of all of that.

Just to highlight how stress can impair your cognition – this is a study done by a few of our research group, not us, but Matthew Lewis who did a PhD with us, David Darby and Paul Maruff, who is one of our psychologists, and they looked at the effect of a full bladder on cognitive status, and the bottom line of this very impressive, highly sophisticated study, which by the way did win an Ig Nobel award, was that if you have got a full bladder you are functioning at about the level of .05; overstress from a full bladder is causing .05. So when you are driving along next time and you have got a full bladder I suggest you stop.

So we have a community who are coming to have anaesthesia - so that is stress, that is the impact of stress and how it affects cognition. We've got a community who are coming to have surgical procedures and they have already got some things happening to them. They may be already confused, they may already have pre-clinical forms or even dementia, and they come along and they have surgery and anaesthesia, hospitalisation, and there are a number of these things which could occur to them in the post-operative period. You may have noticed

this in some of your older relatives.

There may be delirium, which is an acute disorientation syndrome. It can come on in minutes and last for days, it is reversible, but as you will see quite devastating. There may be what we called post-operative cognitive dysfunction which is – it can be early or it can be late, and which is much more subtle, and then what we are really concerned about in our research now is long term cognitive impairment, is there an impact of this going into the long term, which might be either MCI, which is an early form of dementia or dementia itself.

Look at delirium – if you look at all the different types of procedures that we have here up to 50 or 60 per cent of elderly patients may experience delirium in the post-operative period. The problem is it is often unrecognised because everyone knows the agitated patient plucking at butterflies, screaming out, pulling out their tubes and catheters, is delirious, they are disoriented, they are no longer aware of their proper time and place, but at least half of patients actually have what is called hypoactive delirium. It means that they are just sitting there quietly, look terrific, the model patient. They are with the butterflies, they have got no idea what is going on. They are not able to comply with physiotherapy or rehabilitation, so they do not do well either, and this hypoactive form of delirium is often undiagnosed and patients are even discharged from hospital with hypoactive delirium, and a lot of research has demonstrated that if you have an episode of delirium you do worse. It maybe a marker of some degree of cognitive impairment or it may be the delirious, the episode of delirium itself increases

your risk.

One of the things which is of concern is that there is an increased risk of dementia in those who have delirium, and those who have dementia are more likely to get delirium. So we really want to prevent delirium if you are already cognitively impaired, and this comes to a theme, which we'll run through this, is knowing what a person is like before they come to anaesthesia and surgery, because I will reassure you now that if you are cognitively well at the moment going into these procedures you are more likely to do better. You are also more likely to do better if you are under 20, but we will just move past that one.

So to manage delirium there is a whole lot of strategies we can use. We identify the risk, again knowing what they are like beforehand. We can modify triggers and we can treat it, there are certain drugs we can do - but one of the studies which was interesting looked at having a calm, reassuring, relaxing environment as patients were waking up from their anaesthetics. So they installed a harpist in the recovery room. Guess what patients thought when they woke up hearing the harp music. So slightly more stressful.

Moving on to POCD or post-operative cognitive dysfunction, there are two forms which we like to define, which is early and late, and this was picked up after cardiac surgery to start off with by a number of authors, but in particular Pamela Shaw in 1987 who identified that compared to non-cardiac surgery patients having coronary bypass surgery had two to four times the incidence of neuropsychological adverse outcomes; confusion, agitation.

They lumped delirium into that group as well, we would not necessarily do that now, and the tests were different to what we do now. They identified that there was a high risk of neuropsychological adverse outcome after this type of surgery, and everyone thought, okay, cardiac surgery, not a problem for anything else, just cardiac surgery.

Just to clarify what this is POCD is not something you would normally notice. The emails we get are an infrequent manifestation of POCD, mostly subtle change in cognitive function following anaesthesia and surgery measured by neuropsychological tests. It may not be apparent in your eye in the normal course of events. If you were sitting a Gamsat or some other big exam a week after anaesthetic it might be a bad all in this context, but you would not notice if you were not testing it.

So what are we measuring? Well, we put patients through a range of neuropsychological tests, we get them to join the dots form 1 to 8, 2 to B, 3 to C, 4 to E, and so on, on a trails test, we get them to match shapes to numbers, we get them to put little pegs in a grooved pegboard. We time these tests, we check the accuracy, and with a battery of about eight tests we compare them to their previous state and follow the change compared to a control group. We can assess whether they have changed.

So it would be something like this; you come into your operation, you are functioning at this level of cognitive function, you have your operation, your anaesthetic, and then a good group, a normal group bounce back. By about day 90 they are terrific, back to normal. Whereas the impaired group, the POCD group, are functioning at a much lower level, say 30 or so. Everyone

blamed the heart/lung machine in the 70s and 80s, that was probably a reasonable thing. You go to have your heart surgery you are put on a pump. It circulates your blood around this pump and puts it back in your body and surely that is not good for you, it does not seem natural, so it has got to be bad, but we have done a lot of things since then. We have bio compatible filters, we have circuits which are coated with stuff to stop clots and fibrin forming, and I think we have got our act together a lot better.

Interestingly enough Diederik Van Dijk in 2002 was undertaking surgical research because there was a new marketing push, there was a marketing push particularly in the United States to say have your heart surgery done without a heart/lung machine. If you have got coronary artery surgery we can connect up all these things onto the surface of your heart to stabilise it so the surgeon can do the bypass grafts without actually putting you on a heart/lung machine and stopping it. A great idea, and it is going to protect you from having a brain injury. You are not going to have cognitive dysfunction after, and that was actually a marketing point, and Van Dijk was sponsored by the company that makes these devices. In conducting a research project he found there was no difference. There was no difference in cognitive outcome after cardiac surgery on bypass or off bypass, and that is been confirmed in large meta-analyses now looking at a number of different patients, a number of different studies, thousands of patients. From the point of view of cognitive outcomes there are a few other minor benefits like decreased blood loss and possibly decreased stroke,

but that depends on patient selection. From a cognitive outcome point of view it is not happening. It is not a difference, there is no difference, something else is going on.

I just want to reassure you this is another different sort of meta-analysis. We have looked at the trend to a change overall, and the different coloured lines basically show that this is time from early at the bottom right up to late, and on the right is good. It means that overall patients improve after their cardiac surgery. You get better function, you get better performance, overall you improve. What we are looking at is that other group of patients, the ones that John West had trouble with, the ones who do not do so well, and you can't just pool all the results together, you have actually got to tease out those who are affected.

There have been a number of studies looking at non-cardiac surgery, and interesting enough if you review the literature you find the rate at three months of POCD in older patients having non-cardiac surgery is about the same as cardiac surgery, around about 10 per cent or 14 per cent. We did our own analysis, and this is one of the pivotal papers that has come out of recent years from our group, which compared with the same tests, the same investigators, the same assessors, the same statistical analysis, the same control group, coronary artery surgery, hip joint surgery and coronary angiography, going into the cath lab to have your quick coronary angiogram, a sedation procedure, and we identified that at day seven cardiac surgery certainly you have more POCD.

The early POCD is probably related to the drugs and

wearing off and acute phase of the procedure, but by three months there is no difference in POCD between these extremely different stimuli levels of procedure, something else is going on. It does matter, POCD does – may cause subjective complaints like our emails, it may increase your length of stay in hospital. Measurably it decreases your quality of life and some studies have suggested it is even associated with mortality. It is possibly of a limited duration, but I would draw a distinction between the early effects and the late effects. The early effects will improve and late POCD probably improves as well. What we do need to clarify is who is at risk of this sort of thing, and basically obviously those having anaesthesia and surgery, those who are older and those who have less education. So the more education you have the more cognitive reserve you have, less risk you have of these sort of events.

What we need to move into is looking at things like stress and inflammation, these other things which are generic to having a procedure in hospital and not just the anaesthesia and surgery, and that brings us to the last part of this conversation is long term cognitive impairment. What about these sort of events which might impact on mild cognitive impairment or even dementia, and there was an international working group looking at the evidence of there being some impact of anaesthesia and surgery on long term outcomes, and concluding that a durable cognitive decline after elderly exposure may occur in some patients.

As I have mentioned mild cognitive impairment is present in the community over 65. Ten to 15 per cent of

the population have some form of mild cognitive impairment as assessed by a psycho geriatrician, and that increases your rate of progressing to dementia by about ten times. Dementia is obviously horrible, it is a loss of the person. It is an impairment of brain functions including language and memory and personality. It is a complete erosion of the person and it is something we would really like to avoid if we could. It is increasing in the population at the moment. By 2050 there will be over a million people in Australia who have dementia. 2010 was an interesting year, the first of the baby boomers started to turn 65, and by 2020 it is estimated that 75,000 baby boomers will have dementia. It is the fastest growing major disease burden. So anything which even slightly affects the likelihood of progressing to dementia needs to be investigated as a matter of public health priority.

Just a little bit of neurophysiology – so those red things down there are your hippocampus. Hippocampus is sort of like the gateway to memory in the brain, and it is involved with memory and coding and long term recall and spatial orientation, working out where you are, and a lot of the tests we do from memory relate to being able to navigate; mostly if you are a rat, mostly if you are swimming in a pool, but nonetheless navigating.

Alzheimer's Diseases affects the hippocampus and other parts of the brain because of proteins that get deposited in the brain. Amyloid proteins – we do not know what triggers that process, but we do know that the presence of Amyloid proteins and angles within the nerve cells themselves are associated with cell destruction, cell damage and decreased cellular function. We can

measure those by sampling the CSF in the spinal fluid for instance, and if we do sample that spinal fluid or image the brain with scanners such as Chris Rose got at The Austin you can see that Amyloid, this red line here, actually starts to be deposited in the brain perhaps even decades before the clinical onset of symptoms which occur much later from – you know, this is mild cognitive impairment, this is dementia, but before the clinical symptoms appear. So what we are saying is it is a bit like heart disease – it is not the atheroma – well before it starts to cause your heart disease.

The other thing to remember whenever you are talking about these sort of memory functions is that you have good days and you have bad days. So whilst your cognitive – if you think the X axis is severity of cognitive disorder and – sorry, the X axis is time, the Y axis is severity of disorder, over time, yes, there may be an inexorable decline, but you will have good days and bad days, and anyone who has someone, a loved one with any form of impairment will know this. So it is important when we are testing and doing these studies that we have a long term view.

What we are interested in is whether this event of anaesthesia and surgery, instead of it being - you are just on a constant flat level of cognitive function it is actually declining, so that you are already on a decline and then you have your event, stressful event, and you decline even more steeply. I am not going to go through this in any detail, but just to say there is a lot of laboratory data out there which is associating some of the anaesthetics we have with those chemicals that I talked

about, the Amyloid and the tau protein in Alzheimer's Disease, and if that is the case we need to be looking at those anaesthetics and seeing if they change the outcome.

What is a little bit confusing, a lot confusing is the anaesthetics which maybe are associated with more POCD are the opposite, it might be true for those who - that the laboratory evidence says might be associated with Alzheimer's Disease. So we have not got a one size fits all answer, and in fact one of the large researchers in St Louis in the United States, Mike Lavadan, did a retrospective analysis of memory clinic patients who had surgery and anaesthesia and found there wasn't actually - he did not see a strong association with anaesthesia. It was a retrospective study which has always got weaknesses in a group analysis which as I have mentioned is not picking out those ones who are actually deteriorate.

So we hopped on our bikes, well actually Liz hopped on her bike, and drove around Victoria and assessed our patients five to ten years after they have had their cardiac surgery. We went to their homes. These little arrows, that is a map of Victoria there and those little flags are where our patients reside from one of our earlier studies looking at cognition and cardiac surgery, and visited these patients at their homes to see how they were functioning, to do these tests, sit down with them and run these tests in their comfortable home environment and to get some data. What we found opened up some areas for future research and it could be argued to suggest mild concern. But after non-cardiac surgery there might be an increase of up to three or four times a likelihood in those who are at risk of progressing to very mild

dementia, and remember I am talking about this bumpy curve which fluctuates up and down. Even the sedation procedures and cardiac procedures at ten years 33 per cent of patients, which is about three times what your expectation might be, might have some form of very mild - and we talk about very mild, just the beginning of the wedge. Of course some patients severely deteriorate, but overall this is an indicator for further research.

So you get this in the news. I am sure all of you have been at some time a headline in the newspaper and you know it is inaccurate. This was in the news following the Barcelona, the European Society meeting which said that anaesthesia can triple the risk of dementia. I would argue that the author of this article had dementia, because yes the abstract said there was association with anaesthesia and dementia in the three city study in Europe, in France, but the incidence was 30 per cent higher.

Now 30 per cent higher is not tripling the risk, so there is a whole huge cognitive dissidence going on there. Nonetheless they did associate, this is in contradistinction to what the Americans found, that general anaesthesia was associated of an increased risk of dementia over the period of this study which was about eight to ten years. New information, very early data, still looking at mechanisms and still looking at risk factor. So it is something to do with anaesthesia in patients who are already vulnerable, have already got the Amyloid disease of Alzheimer's. Plus some sort of trigger, maybe it is inflammation, maybe it is surgery, maybe it is the anaesthetic. We know from pain medicine

that all the little cells around the neurons the glia are actually really active, and they are inflammatory cells, and sparking them up an can increase celluloid damage. Now if you increase the damage in inflammation in the brain you might increase the risk of cognitive impairment, and there is a lot of work going on into glial modification at the moment.

So if we put it together, we say, well okay you go into your operation. Everyone who has an operation will have some sort of inflammatory response, some sort of stress response. If your microglia are resting and normal and your blood brain barrier, your brain health is good, everything is fine. If you have got some weakness in your blood brain barrier due to prior cognitive illness or prior inflammatory condition this could be amplified. It is just like going to hospital already having some coronary artery disease or some angina and having an increased risk of heart attack. The same story. It is exactly the same paradigm.

These are just graphs showing that inflammatory markers, the chemicals we measure in the blood that indicate inflammation go up through up anaesthesia and surgery, and if you take a rat and you put him in a pond standing on a rock and ask him to remember where the next rock is those rats who you block that inflammatory response from occurring retain their memory much better than those rats who do not after having had a surgical procedure.

So there is laboratory and animal evidence to suggest that if we modify this in some way we might be able to improve outcomes, and as it happens if you measure

these inflammatory chemicals in patients having just general anaesthesia on the left here versus having general and regional anaesthesia you see that if you just have general anaesthesia your inflammatory bio marker as I said goes sky high, the stress of the surgery and the response. If you block the pain the only ones which go up are the protective ones. It is a reverse mirror image of the pattern that happens. So if you are offered an epidural anaesthetic for instance to go with your bowel surgery take it, it might well be something which decreases the inflammatory response associated with it.

Indeed if you are having hip surgery and I have highlighted there delirium is reduced by having a regional anaesthetic, so a spinal anaesthetic. If we can block the stress response we might be able to improve some of these cognitive outcomes. Now, none of you have probably been down to St Kilda lately, but there is a drug on the streets called Vitamin K Ketamine. Well we have known about that for decades, we use it with anaesthetics all the time. It is a very useful analgesic agent in low doses. It does call hallucinations in moderate doses and does cause anaesthesia in high doses. What is interesting is it is an anti-inflammatory drug and it is an atypical type of anaesthetic, and some studies would suggest that this drug decreases the instance of delirium and adverse outcomes consequent of that. Again very early days; we have put in a bid to be funded for this research this time around and if any of you have got influence with the NHMRC now is the time to wield it.

Back to the reassuring stuff. There is a whole story about anaesthesia and neonatal developing brains.

This is a different story. I am not an expert in that area, I am not going to discuss it, and mostly it is not a problem. In mid life, which we all are, we have a large cognitive reserve, we have limited exposures, we have good function and anaesthesia in surgery poses us no substantive cognitive risk by and large.

If on the other hand you are vulnerable, you are the impaired elderly, you have got some neuropathology, you have an inflammatory response, they are the group that we are interested in targeting with our current research to try and develop a strategy so we can identify them, perhaps guide surgery choice, guide anaesthesia type, protect them and get better outcomes. So what we can do is we can screen patients effectively, we are looking for the Judy Dench rather than the Ronald Reagans to see how they go, and just a bit like having your pre-operative ECG or your pre-operative blood test for your haemoglobin we need – we haven't got yet, we are looking for a pre-operative test which we can just apply and screen, find people who are at higher risk which is effective, reliable and convenient.

There is this great quiz at St V's which is a patient personal profile and it is headed "Information about me" and I thought this is for me to fill in if I am doing it. Then if you start reading it, "I can ask for something if I need it? Yes, I can." You get down here, "I can be verbally aggressive? Yes" – I am not going to say yes. "I can be physically aggressive. I wander and try to leave the house." Who is going to fill this out, and then I realised it was actually for the spouse to fill in for their partner.

So that is one way of assessing, but basically there is a use it or lose it philosophy, and I just warn you this is getting close to the end, it is also an evidence free zone. You have got to protect the milieu, the environment, the brain. So you avoid toxins and traumas, so I have instructed the waiting staff not to serve any more alcohol tonight, if that is okay. We have got to protect the cortex, we can do exercises, Sudoku is better than crosswords you will be interested to know, because crosswords are long term retention and Sudoku is current creative said chess is very good as well.

Then there is that hippocampus. Now hippocampus is that red stuff that was in that rotating skull. That is the memory gateway in the brain and the hippocampus of patients with Alzheimer's Disease shrinks, it gets smaller from the neuronal degeneration. You can do an aerobic exercise, that will improve your hippocampus. The other thing is your hippocampus is all to do with finding your way around the maze, finding your way around the maze is mapping.

There was this really interesting study by this Scotsman called Maguire of the London cabbies in the year 2000, and the cabbies have to - do you know what they have to do - they are not like the cabbies in Australia, they have to do a test before they hop in the driver's seat of local knowledge, they call it knowledge, and they have to know the knowledge. He did MRIs, X-rays, complex scans of their brains and found out that those cabbies who used GPS navigation rather than relying on their intrinsic knowledge of the back roads and byroads had smaller hippocampuses. In other words those who were exercising

their map skills do better. So throw away that GPS and your iPhone which takes you off cliffs and things like that and start navigating yourself around as a bit of mental exercise. You might get lost.

Pre-operatively I' hae talked about most of the things we can do. We are trying to learn what tools we can do to intervene, we are very early days yet. It is the connection between anaesthesia and surgery which is important. They are not separate, it is not just that anaesthesia is bad, it is not just surgery is bad. Both of them together achieve a great deal in improving quality of life in a majority of people. We are just looking to try and decrease the potential for an adverse outcome which might impair a smaller proportion of those, those who we have identified.

Finally, afterwards what can you do. Cognitive activities are probably something you can do. If you know someone – this again is low grade evidence, but if you know someone who has got some form of cognitive impairment if you enrich their environment, if you get them doing things it will improve outcome, a more stimulating environment. The older person who has got some impairment who goes home to be on their own sitting in the quiet in the dark will not do well, they will not progress, they will not advance. So it is a mixture of things, it is anaesthesia, it is stress, it is inflammation, all together changing the outcomes. Less so for those who have got good cognitive reserve and at higher risk for those who have got poor cognitive reserve, and we are looking at that particular question in one of our larger studies at the moment called the ahead study which we have

been recently been funded for where we are looking for any volunteers, 264 patients over two years follow up for each patient, so it is a four year study. Those who have got some form of cognitive impairment coming in to having surgery and procedures we are tracking them for over two years to see if they have a change in their outcome and see if we can identify factors which we hopefully modify, and underway at the moment is the first levels of what is called the capacity study where we are taking people who are just coming to have major joint replacements, so hip, knee surgery, having a spinal anaesthetic. I mentioned that those fluid markers in the spinal fluid are the early indicators of Alzheimer's Disease and we are asking them to let us sample that spinal fluid as part of their spinal anaesthetic and then track their cognitive outcomes over time; other areas for research I have mentioned.

Finally I would like to acknowledge profoundly the team, and Liz Everett and Brendan Silbert are the backbone of our research group, the Centre for Anaesthesia and Cognitive Function at St Vincent's, which is just up the road, and have been – this project has been, these various projects have been driving on for well over a decade now, and we have also got Sarah Maher and Sally Pritchard who has left us now and gone to Queensland for God knows what reason, and Frank Mooney. But, you know, you can imagine with a team like that all our patients are very keen to be followed up.

Finally I would just like to reflect on the fact it is better to look forward rather than look backwards. Thank you.

MS LYTHGO: It occurred to me during that that if this all gets

out into the open the medical indemnifiers are going to refuse to let any of us work. We have got at least one member of the Board Avant(?) here tonight. Fortunately he is a surgeon so he needs us. David has offered to take questions from the floor and Michael will be roving with his microphone.

SPEAKER: Thank you very much for that excellent presentation, it was magnificent. I am a general practitioner and a couple of points that you've made here lead me to ask Question 1: What is the role of Aspirin in this sort of reduction of inflammation pre-operatively, for instance in people who are taking it as a protective mechanism; one for, you know, heart disease, prevention or cardiac arrhythmia, whether or not there's a difference in terms of their outcome post-operatively from the anaesthetic, and (2) whether or not there's been any exploration regarding their pre-existing liquid profile for instance in terms of – and other sort of like cardiac disease risk factors and dementia risk factors too, whether or not those two particular elements have been examined.

ASSOCIATE PROFESSOR SCOTT: I am sure you are all over the dementia risk factors which are mostly lifestyle and dietary modification factors, including obviously exercise and choosing the right parents are very important things. The Aspirin question is an interesting one. There is a study called the ASPREE trial, which is underway still, looking at just that question, whether Aspirin modifies outcomes including cognitive outcomes, and we don't know the answer to that yet. I mean Aspirin seems to be the drug that everyone should be on because it cures everything except peptic ulcers. So if you can tolerate

Aspirin probably it's a good idea to be on it for all those reasons, but we don't have the absolute answer to that but this trial, which is being conducted in Melbourne, should hopefully give us some feedback on that. We are not actually actively involved in that.

The question about statins and lipids is interesting, because hypercholesterolaemia in cardiac disease, vascular disease is associated with dementia. Interventions which modify those risk factors should improve the outcome, and that is probably true in a broader sense, but there are some patients who actually get memory problems with statins, and I think this is another example of it's not one size fits all, you've got to realise that some patients have different response to the drugs than others and maybe 80 per cent of patients will have a good response to statins, decrease their cholesterol and their lipids, modify their cardiac risk factors and maybe improve their outcome, maybe, but some patients will actually have memory problems with statins for other reasons, because cholesterol is the insulation on neurons and it might be that interfering with that trafficking actually has an effect.

SPEAKER: (Off microphone).

ASSOCIATE PROFESSOR SCOTT: Well, do you think we should go back to all those things which gave us indigestion.

SPEAKER: (Off microphone).

ASSOCIATE PROFESSOR SCOTT: And just dietary modification as well.

MS STOKER: Anne Stoker – what would be the effect of tranquillisers often used to aid sleep in older people, the ageing brain? Would they be similar to some of the

anaesthetics?

ASSOCIATE PROFESSOR SCOTT: That's an excellent question, and I'm not aware of anything we could say which would tease that out. We do know that benzodiazepines which are the commonest sedatives are more increasingly associated with confusional states in patients. Some of the anti-psychotics which are used to help patients who do have say delirium are probably of great benefit, because they reverse that agitated cerebral state. So I can't answer your question in a simple way. I don't know if Brendan or Liz has anything to add to that. It's sort of speculation. I think it is a good question, and the problem is difficult to tease out, because sleep disturbance is a real plague of the elderly and if you're not sleeping you're not regenerating either and I think to lose that you then go to the sleep physician's expertise and say, well which is good REM sleep and which is good non REM sleep and are you're getting the right balance. The problem probably with benzodiazepines is you don't get the right balance of restorative sleep.

SPEAKER: (Off microphone).

ASSOCIATE PROFESSOR SCOTT: Correct. So if the drug you're using gets you off to sleep and then you have a natural sleep because you're being put off to sleep that's great. The only sleep you're getting is because you need high doses of some sort of sedative. Probably not the ideal situation, but what is the alternative.

MR EDWARDS: Will Edwards, orthopaedics. I have a colleague who had a hip replacement and did a ward round the next morning. In those with good cognitive reserve how long should I tell my patients to stay away from academic work?

ASSOCIATE PROFESSOR SCOTT: Well, your colleague must have had a fantastic anaesthetic clearly. Moving on from that point the tradition has been, you know, 24 hours after you've had an anaesthetic you can start signing your legal documents again and driving cars for minor procedures, and clearly the information that we have got suggests that's not the case after more major procedures, whereas, you know, a week later 47 per cent of patients have got some form of POCD if you measure it. To identify those who are – and at the moment we don't have an exit strategy. You know, the AFL looks at these cognitive test computers to see where the patients after head injury are ready to run back on the field or not, and we don't actually apply those same rules after having had a medically induced coma such as an anaesthetic, and the other complicating factor, Will, of course is if someone's got – I know it wouldn't happen in any of your ankle reconstructions, but some sort of painful surgery after, so pain and they have opiates or other forms of analgesics, then that's going to impact on their recovery profile as well. Obviously the best thing to do is to get up and get moving and functional status as always is our guide. So if someone's up and functioning well then probably cognitively they're functioning well as well. That is a very broad-brush answer and we would love to be able to give you the exact predictor.

MR CEMASK: Thanks, David, my name is Richard Cemask(?), I'm a GP. For many years surgeons have asked patients to stop smoking some weeks before their surgery. Can you make a bit of a comment on the risk factors involved with smoking and what you have been talking about.

ASSOCIATE PROFESSOR SCOTT: Thanks, Richard. I would hasten to

point out that the College of Anaesthetists has put out a position statement on smoking, and you may have picked that up in the media in around about July, where we are strongly advocating the role of anaesthetists is to actually help patients quit smoking, because there's the short and long term advantages to ceasing smoking. So from the point of view of oxygen delivery 24 hours is enough. From the point of view of immune function, one to two weeks, and it's getting back to normal, and by about six months your sputum production has normalised. You know, there is this increase in sputum production after stopping smoking, but the advantages far outweigh the disadvantages in most circumstances.

So I would urge you to go onto the ANZCA website and read the position statement on smoking, which has got an appropriate literature basis behind it, because it is important, smoking is a problem and a challenge and it is a risk factor for Alzheimer's Disease, cognitive impairment, and macula degeneration and all those sorts of things. So there is a lot of good reasons for quitting smoking.

SPEAKER: (Off microphone).

ASSOCIATE PROFESSOR SCOTT: In cognitive decline, no, I could not give you a figure.

SPEAKER: (Off microphone).

ASSOCIATE PROFESSOR SCOTT: We do measure smoking in our patients and usually it spins out of the risk factors by the time we have done our multivariable analyses.

SPEAKER: (Off microphone).

ASSOCIATE PROFESSOR SCOTT: We have old patients who have mostly got a history of smoking; there's just too many of

them.

MS LYTHGO: I think we had better pass on to damaging our brains with a little bit of alcohol now. So I will ask Phoebe to come up and thank David for us.

MS MAINLAND: Well, as an anaesthetist I think I have done my CPD experience for at least the next six months, and one of the things I did pick up was the good days and bad days, I think that is another very good term. I think the idea of memory dysfunction is relevant no doubt I expect to all of us, whether or not it is through contact with a friend, family or personal concerns.

I also appreciated the Kardashians, I've just learnt how to say that, as the information overload. I think in these days where there is so much coming into our brains sometimes there is a challenge of what we can remember, and the old idea of our memory is a box and when it gets full something has to go out the other end. So some of those memory theories I am expecting that the work that David and his team are doing will help not just with teasing out what the issues are after surgery and anaesthesia, but also with their collaborative work help with determining some of the influences on memory in the general population even without those insults, and I use that in a friendly way.

I would like to congratulate David not only on his talk tonight, but also with his team and the work that they have done, and thank him very much for his talk and I think one of the morals of the story is to reduce the impairment before you go to theatre don't turn up drunk. Thank you very much, David.

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